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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/717,246	11/18/2003	Edward William Adams	IVGN 762.2 DIV	7752
56466	7590	07/13/2007	EXAMINER	
INVITROGEN CORPORATION			TSOY, ELENA	
C/O INTELLEVATE			ART UNIT	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/717,246	ADAMS ET AL.	
	Examiner	Art Unit	
	Elena Tsoy	1762	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 18 June 2007.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-17 is/are pending in the application.
 - 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 1-17 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) Notice of References Cited (PTO-892).
- 2) Notice of Draftsperson's Patent Drawing Review (PTO-948).
- 3) Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____.
- 4) Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) Notice of Informal Patent Application
- 6) Other: _____.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on June 18, 2007 has been entered.

Response to Amendment

Amendment filed on June 18, 2007 has been entered. New claim 17 has been added. Claims 1-17 are pending in the application.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

2. Claims 1-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bawendi et al (WO 0017655) in view of Kohn et al (WO 99/24490).

Bawendi et al in view of Kohn et al are applied here for the same reasons as set forth in paragraph 5 of the Office Action mailed on 1/17/2007.

As to Amendment, Bawendi et al show an exemplary bilayer molecule in FIG. 5B in which an inner layer 40 includes a molecule 42 (here TOPO) (claimed quantum dot nanoparticles passivated with a coordinating TOPO solvent in which they were prepared) having a linking moiety 44 with an affinity for the semiconductor surface and a hydrophobic tail 48 extending from the linking moiety (See column 17, lines 45-49). The second outer layer 50 is comprised of inner hydrophobic region 52 and a terminal hydrophilic moiety 54 for favorable interaction with an aqueous medium (See column 17, lines 49-52). The hydrophobic regions 48, 52 of the inner and

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outer layers, respectively, interact preferentially in the aqueous medium, to form a **micelle encapsulating** the nanocrystal therein (See column 17, lines 52-57). The water-dispersible semiconductor nanocrystal shown in FIG. 5B may be prepared by adding a surfactant such as sodium dioctylsulfosuccinate (trade name AOT) (amphiphatic dispersant) to a solution of TOPO-capped CdSe(ZnS) semiconductor nanocrystals in **hexane** (claimed non-aqueous non-polar solvent) to give a solution (claimed step a of admixing dispersant and nanoparticles in non-polar solvent); evaporating hexane under vacuum (claimed step b of causing adsorption of the dispersant by the nanoparticles); and dissolving the resulting solid residue in water to give a clear solution (claimed step c) (See Fig. 5B and Example 4).

Bawendi et al fail to teach that a polymer having **two or more** alternating hydrophobic and hydrophilic regions can be used for the **micelle encapsulation** (Claim 1).

Kohn et al teach that a polyether surfactant comprising strictly alternating poly(alkylene oxide) and aromatic diol monomeric repeating units (See column 2, lines 22-27) so that *hydrophilic and hydrophobic regions are distributed uniformly* along the polymer chain (See column 4, lines 60-63) form self-assembled **micelles** having hydrophobic interiors into which hydrophobic drug particles are incorporated and hydrophilic exteriors which maintain a stable dispersion in aqueous media (See column 1, lines 32-35; column 2, lines 13-21) when mixed with *hydrophobic* drug particles in water (See column 4, lines 55-65; column 9, lines 60-63) thereby forming stable aqueous polymeric **surfactant** dispersions (See column 10, lines 65-67; column 14, lines 1-3). In other words, Kohn et al teach that a polymer having hydrophilic and hydrophobic regions uniformly distributed along the polymer chain is suitable for the use as surfactant for forming self-assembled **micelles** having hydrophobic interiors into which hydrophobic particles are incorporated and hydrophilic exteriors which maintain a stable dispersion in aqueous media thereby forming stable aqueous polymeric surfactant dispersions of hydrophobic particles. Obviously, one of ordinary skill in the art would have reasonable expectation of success in using a polymeric surfactant of Kohn et al for dispersing **any** particle as long as it has a hydrophobic surface for interaction with a hydrophobic portion of the surfactant.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to have used a polymer having hydrophilic and hydrophobic regions uniformly distributed along the polymer chain as surfactant in Bawendi et al instead of AOT with the expectation of

forming *micelle* via interaction of a terminal hydrophobic region of the polymer with hydrophobic tail 48 of the inner layer 40 thereby providing stable aqueous polymeric surfactant dispersions of hydrophobic nanoparticles since Kohn et al teach that a polymer having hydrophilic and hydrophobic regions uniformly distributed along the polymer chain is suitable for the use as surfactant for forming self-assembled **micelles** having hydrophobic interiors into which hydrophobic particles are incorporated and hydrophilic exteriors which maintain a stable dispersion in aqueous media thereby forming stable aqueous polymeric surfactant dispersions of hydrophobic particles.

As to claim 17, Bawendi et al teach that any material comprised of moieties with affinity for the nanocrystal surface and moieties with affinity for the aqueous medium stabilizes the semiconductor nanocrystal suspension (See column 13, lines 1-22).

Kohn et al teach that a polyether polymer having strictly alternating hydrophilic and hydrophobic regions are distributed uniformly along the polymer chain decrease the surface adhesion of the polyether to cell and are useful as non-thrombogenic coatings on surfaces in contact with blood (See column 4, lines 66-67 to column 5, lines 4). The polyether also resists bacterial adhesion in this, and in other medical applications as well (See column 5, lines 4-5).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have used any molecule comprising moieties with affinity for the nanocrystal surface and moieties with affinity for the aqueous medium including a polyether polymer with *randomly* alternating hydrophilic and hydrophobic regions as a dispersant in Bawendi et al with the expectation of providing the desired stable suspension of quantum dot nanoparticles if the nanoparticles are not for introducing into body.

3. Claims 1-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bawendi et al (WO 0017655) in view of Ma et al (US 5,221,334).

Claims 1-16 are obvious over Bawendi et al in view of Ma et al for the reasons of record set forth in paragraph 6 of the Office Action mailed on 1/17/2007 and for the reasons discussed above.

Bawendi et al teach that any material comprised of moieties with affinity for the nanocrystal surface and moieties with affinity for the aqueous medium stabilizes the semiconductor nanocrystal suspension (See column 13, lines 1-22).

Ma et al teach that copolymers having hydrophobic and hydrophilic regions where a hydrophobic unit serves to link with a hydrophobic pigment, and the hydrophilic region serves to disperse the pigment in the aqueous medium (See column 3, lines 26-34) is suitable for stabilizing a *hydrophobic* pigment of 0.005-1 microns (5 nm-1000 nm) (See column 7, lines 25-27) in an aqueous medium over long periods (See column 3, lines 15-17). The block copolymers may be either of AB or BAB block copolymer where A is hydrophobic block and B is a hydrophilic block (See column 3, lines 27-30) such those shown in the Table (See column 5, lines 23-65). Obviously, one of ordinary skill in the art would have reasonable expectation of success in using copolymers of Ma et al for dispersing *any* particle as long as it has a hydrophobic surface for interaction with a hydrophobic portion of the copolymer.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to have used block copolymers having hydrophobic and hydrophilic blocks as a dispersant in Bawendi et al with the expectation of providing the desired stability of aqueous dispersion of nanoparticles since Bawendi et al teach that any molecule having at least one hydrophobic linking moiety that attaches to the surface of the particle and that terminates in at least one hydrophilic moiety may be used as an outer layer, and Ma et al teach that a block copolymer having hydrophobic and hydrophilic blocks may be used as dispersant by linking to a hydrophobic particle via a hydrophobic region.

As to claim 17, Ma et al teach that a *random* polymer of hydrophobic and hydrophilic monomers may be used for dispersing a hydrophobic pigment in an aqueous medium (See column 17, line 61 to column 18, line 40). However, ink printed irregularly on the thermal inkjet printer compared to ink made with a block copolymer dispersant (See column 18, lines 41-45).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to have used *random* polymers of hydrophobic and hydrophilic monomers as a dispersant in Bawendi et al with the expectation of providing the desired stability of aqueous dispersion of nanoparticles since Bawendi et al teach that *any* molecule having at least one hydrophobic linking moiety that attaches to the surface of the particle and that terminates in at least one hydrophilic moiety may be used as an outer layer, and Ma et al teach that a random polymer of hydrophobic and hydrophilic monomers is suitable for dispersing a hydrophobic particle in an aqueous medium.

Response to Arguments

4. Applicants' arguments filed June 18, 2007 have been fully considered but they are not persuasive.

I. Claims 1-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bawendi et al (WO 0017655) in view of Kohn et al (WO 99/24490).

Applicants argue that in the Office Action mailed on 8/31/06, the Examiner noted that Bawendi describes nanocrystal structures with a TOPO inner-coating and further having an outer surfactant coating such as AOT with a hydrophobic region and a terminal hydrophilic moiety (referring to Fig. 5B in US 6,319,429). The AOT forms a bilayer around the internal nanocrystal, with polar head groups facing out, thereby rendering the particle water soluble. The Office Action acknowledges that Bawendi does not describe a polymer as claimed, but asserts that the polymers in Kohn fill that void. Kohn "relates to strictly alternating poly(alkylene oxide ether) copolymers that self-assemble in aqueous media to form micelles that are useful for the delivery of hydrophobic drugs." Emphasis added, Page 1, Technical Field. The combination of Bawendi and Kohn yields a fundamentally different preparation than claimed (i.e. one formed in aqueous solvents). Furthermore, if the Examiner's argument is that Kohn poly(alkylene oxide ether) copolymers can form micelles in nonaqueous, nonpolar solvents, Applicants request that specific supporting evidence be made of record, as such theory seems contrary to the description in Kohn. In view of the foregoing, withdrawal of the obviousness rejection to Claims 1-16 over Bawendi in view of Kohn is respectfully requested.

The Examiner respectfully disagrees with this argument. The method described in primary reference of Bawendi comprises all three steps a)-c) (See paragraph 2 above), as claimed and as described in Applicants' Example 2, where dispersant and nanoparticles are admixed in a solvent, the solvent is evaporated under vacuum, and then the residue is dispersed in water. Kohn et al is a *secondary* reference which is relied upon to show teach that a polymer having hydrophilic and hydrophobic regions uniformly distributed along the polymer chain is suitable for the use as surfactant for forming self-assembled **micelles** having hydrophobic interiors into which hydrophobic particles are incorporated and hydrophilic exteriors which maintain a stable dispersion in aqueous media thereby forming stable aqueous polymeric surfactant dispersions of

hydrophobic particles. Obviously, one of ordinary skill in the art would have reasonable expectation of success in using a polymeric surfactant of Kohn et al for dispersing *any* particle as long as it has a hydrophobic surface for interaction with a hydrophobic portion of the surfactant.

Thus, in contrast to Applicants argument, the combination of Bawendi and Kohn yields a preparation substantially identical to that of claimed invention.

II. Claims 1-16 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Bawendi (WO 00/17655 or US 6,319,429) in view of Ma et al. (U.S. Patent No. 5,221,334).

Bawendi describes nanocrystal structures with a TOPO inner-coating and further having an outer surfactant coating such as AOT with a hydrophobic region and a terminal hydrophilic moiety (referring to Fig. 5B in US 6,319,429). Ma requires that "[t]he ink is prepared by premixing the selected pigment(s) and acrylic block copolymer in water, a water soluble medium solvent, or the aqueous carrier medium." In fact, the polymer and pigment in Ma are selected based on their ability to form an ink in an aqueous solution. Column 3, lines 25-35. Nowhere in Ma or Bawendi is there any description of a preparation as presently claimed. In fact Ma, explicitly states that the premixing be done in aqueous/polar solvents and specifically formulates the block copolymers based thereon. Premixing the passivated hydrophobic quantum dot nanoparticles in a polar aqueous solvent, as required in Ma's method, is not claimed. With respect to new claim 17, Ma describes AB or ABAB copolymers which are uniformly dispersed throughout the polymer. Ma describes "random polymers" as a negative control to show the purported superiority of the uniform AB or ABAB copolymers described therein. Column 17-18. Accordingly, Ma teaches away from the use of random polymers wherein the hydrophilic and hydrophobic regions are randomly interspersed.

The Examiner respectfully disagrees with this argument.

As to Applicants' statement "Premixing the passivated hydrophobic quantum dot nanoparticles in a polar aqueous solvent, as required in Ma's method, is not claimed", First of all, claims do not exclude a step of premixing the passivated hydrophobic quantum dot nanoparticles in a polar aqueous solvent or recite negative limitation of not premixing. Secondly, Ma et al is a **secondary** reference which is relied upon to show that copolymers having hydrophobic and hydrophilic regions where a hydrophobic unit serves to link with a *hydrophobic* particle, and the

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hydrophilic region serves to disperse the pigment in the aqueous medium **is suitable** for stabilizing a *hydrophobic* particle in an aqueous medium.

Thirdly, Ma teaches away from the use of random polymers wherein the hydrophilic and hydrophobic regions are randomly interspersed for making **ink** compositions in diethylene glycol and water.

One of ordinary skill in the art would have reasonable expectation of success in using random polymers of Ma et al since Bawendi et al teach that *any* molecule having at least one hydrophobic linking moiety that attaches to the surface of the particle and that terminates in at least one hydrophilic moiety may be used as an outer layer, and Ma et al teach that a random polymer of hydrophobic and hydrophilic monomers is suitable for dispersing a hydrophobic particle in an aqueous medium.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elena Tsoy whose telephone number is 571-272-1429. The examiner can normally be reached on Monday-Thursday, 9:00AM - 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Timothy Meeks can be reached on 571-272-1423. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Elena Tsoy
Primary Examiner
Art Unit 1762

ELENA TSOY
PRIMARY EXAMINER
ETSOY

July 10, 2007